

FIGURE 1

Consensus

re3 (15-45)
 hcj7.pep (15-45)
 nv1.pep (15-45)
 GE11.2 (15-45)
 s71957.p (15-45)
 ec10 (15-45)
 sp2.tc (15-45)
 M2.2 (15-45)
 rela (15-45)
 168 (15-45)
 M1.5 (15-45)
 hpcprc1a.p1 (14-44)
 gm2.tc (15-45)
 s71864.p1 (15-45)
 i15.tc (15-45)
 sp1.tc (15-45)
 re37b (15-45)
 re39 (15-45)
 hpchcj2.p (15-45)
 hpccgenom.p1 (15-45)
 hpcprc4a.p2 (14-44)
 hpcprc11a.p1 (4-34)
 re72b (15-45)
 hpcprc3a.p1 (4-34)
 re70 (15-45)
 re42 (15-45)
 63 (15-45)
 hcvj (15-45)
 hcvj1 (15-45)
 re38 (15-45)
 bk (15-45)
 re5 (15-45)
 re35 (15-45)
 re36 (15-45)
 re54 (15-45)
 re56 (15-45)
 64 (15-45)
 re62 (15-45)
 re41 (15-45)
 hpcvj3.p (15-45)
 jk2 (15-45)
 hcv1 (15-45)
 us5.tc (15-45)
 i21.tc (15-45)
 M3.1 (15-45)
 H77 (15-45)
 re43 (15-45)
 Ge6.3 (15-45)
 CO11 (15-45)
 TH (15-45)
 O115 (15-45)
 re4a (15-45)
 q1 (15-45)
 q3 (15-45)
 gh1.tc (15-45)
 M4.1 (15-45)

.T.VTGG.AARTT.G..SLF..G.SQ.IQLI

A.YA..AAQGHA.NSFV...RS.A..NLK.V
 S.Q....Q..H.VR.VA.I.SP.SR.D.S..
 S.R....QQG.AVH.IA...SL.A..K...V
 S.H.M.AQQG.VAK.FT...GP.PA.K....
 S.H...AVQGSIR.LT...TS.PA.K...V
 E.H....I..K..ASLTG..NL.AK.N....
 E.H....N.G.AAA.IAG..TL.AK.NV...
 Q.R....T..QS.ARIAG..SL.AR.N....
 Q.H.M..T.G.NAY.LT.FLSV.A..K....
 E.H.M..A.SS..YRFA...TS.PA.K...V
 E.H....S..S..ATFSK..MP.A..N....
 G.TRV..A.....SSFA..LTH.P..N...V
 G.H....A...DAFRFS...TR.P..N....
 A.NM...AP....YKLT..SY.A..K....
 HNH....TS..N.F.ITT..TQ.P..KL..V
 G.H....A...NAHSLT..LAP.A..K....
 T.R.S..T..H..A.LT...SP.PR.N.H.V
 T.H.S..T.G...ASLT.F.AP.A..R...V
 T.H....ATGH..S.IA...LP.A..K....
 D.YAS..AQG.S.L.FT...TP.A..K....
 D.YAS..A.G.A.Y.IT...AP.A..N....
 R.YAS..A.G...H.FT...ST.AR.N....
 Q.Y....K..Q.VS.FTG..SS.P..K....
 D.Y.S..A...SIS.FT...TP.A..K...V
 S.Y....E.S...R.FA...TL.S..K....
 N.Y....S.G.AVA.FAG.LQP.AK.NV...
 H.R....QV.FR.H.LV...TQ.P..K...V
 H.H....RV.SS.QSLV.WLSQ.P..K...V
 H.R....VQGHV.STLT...RP.A..K...V
 N.R....VQG.D.S.LV...SL.P..K...V
 D.H....AQ.K..NRLV.M.AS.P..K....
 E.H....AS....QRFT.F.DL.P..K...V
 T.YM...AN....Q.FV...TP.PA.K...V
 E.H....TS....Q.FV...SA.A..K...V
 G.H....Q.....QSFT...SP.PQ.K....
 R.H....K..H..K.FA...TP.P..N....
 E.R...AVQGHGAL.LA...TP.P..K....
 E.R...AI.G..ASSFAG..TS.A..K...V
 E.R...QVQ...QSLT...TP.P..T....
 Q.R...AQVG...SSLT...TP.P..N...V
 R.Q...AQ.GH..S.LA...TP.P..K...V
 E.H....S.GH.VS.FV..LAP.AK.NV...
 E.H....S.GH.VT.IA...TS.AK.N....
 S.H....T..H.VA.FS...TV.PK.N....
 E.H....A..Y.AA.LA...TS.AK.N....
 E.H....S.G...A.LVG.LTP.AK.N....
 G.H....S.G.A.A.IAG.LTP.AR.N...V
 K.H....S.....S.IA..LTP.AK.NV...
 K.Y....SQ.QA.F.FT..LQP.AK.N....
 E.T....S..HGAL.IA...NQ.AR.N....
 E.Y....AS..S.FTLVG..KQ.SQ.N...V
 Q.Y.S..SSG...S.LV.I.SP.A..NL...
 E.Y.S..A..Q..ARFAGF.QS.AK.N....
 E.Y.S..S..Q..A.FVR..ET.PK.N....
 S.Y.S..AQ..AAQ.IT...SR.S..K...V
 S.Y....TQG.AAS.LT...SA.A..N....

FIGURE 2-1

31 (SEQ ID NO: 8)

45 (SEQ ID NO: 9)

45 (SEQ ID NO: 10)

45 (SEQ ID NO: 11)

45 (SEQ ID NO: 12)

45 (SEQ ID NO: 13)

45 (SEQ ID NO: 14)

45 (SEQ ID NO: 15)

45 (SEQ ID NO: 16)

45 (SEQ ID NO: 17)

44 (SEQ ID NO: 18)

45 (SEQ ID NO: 19)

45 (SEQ ID NO: 20)

45 (SEQ ID NO: 21)

45 (SEQ ID NO: 22)

45 (SEQ ID NO: 23)

45 (SEQ ID NO: 24)

44

34 (SEQ ID NO: 25)

45 (SEQ ID NO: 26)

34

45 (SEQ ID NO: 27)

45 (SEQ ID NO: 28)

45 (SEQ ID NO: 29)

45 (SEQ ID NO: 30)

45 (SEQ ID NO: 31)

45 (SEQ ID NO: 32)

45 (SEQ ID NO: 33)

45 (SEQ ID NO: 34)

45 (SEQ ID NO: 35)

45 (SEQ ID NO: 36)

45 (SEQ ID NO: 37)

45 (SEQ ID NO: 38)

45 (SEQ ID NO: 39)

45 (SEQ ID NO: 40)

45 (SEQ ID NO: 41)

45 (SEQ ID NO: 42)

45 (SEQ ID NO: 43)

45 (SEQ ID NO: 44)

45 (SEQ ID NO: 45)

45 (SEQ ID NO: 46)

45 (SEQ ID NO: 47)

45 (SEQ ID NO: 48)

45 (SEQ ID NO: 49)

45 (SEQ ID NO: 50)

45 (SEQ ID NO: 51)

45 (SEQ ID NO: 52)

45 (SEQ ID NO: 53)

45 (SEQ ID NO: 54)

45 (SEQ ID NO: 55)

45 (SEQ ID NO: 56)

45 (SEQ ID NO: 57)

45 (SEQ ID NO: 58)

45 (SEQ ID NO: 59)

45 (SEQ ID NO: 60)

45 (SEQ ID NO: 61)

45 (SEQ ID NO: 62)

45 (SEQ ID NO: 63)

45 (SEQ ID NO: 64)

nac5.tc (15-45)
 hpcgenanti.p3 (15-45)
 hcj4 (15-45)
 hpchcv.p2 (15-45)
 hcj1 (15-45)
 hct18 (15-45)
 hct27 (15-49)
 hcvel (15-45)
 gel2 (15-45)
 LG (15-45)
 jt.p3.x (15-45)
 us4.tc (15-45)
 jk1 (15-45)
 hpcvjk4.p (15-45)
 hpce2cor.p (15-45)
 hpcns34d.p (15-45)
 FTO.1 (15-45)
 Gj6.1 (15-45)
 re7 (15-45)
 hcvkf (16-46)
 arg2.tc (15-45)
 hcj6 (15-45)
 hpchcj5.p (15-45)
 rs1.pep (15-45)
 re71 (15-45)
 re6 (15-45)
 hcj8.pep (15-45)
 re40 (15-45)
 hpcencr.p (15-45)
 re55b (15-45)
 aus1.tc (15-45)
 PC2.1 (15-44)
 hct23 (15-45)
 re34 (15-45)

N.Y.S..T.GH.GH.LTA..SP.A..N....
 S.I.S..TV....HSLA...TQ.A..K....
 E.YTS..A.SH..STLA...SP.A..R...V
 H.LT...H...L.S.FAG..TP.P..R....
 E.I.S..Q...AMS.LV...TP.AK.N....
 E.YTS..N.GH.MT.IVRF.AP.PK.NVH..
 T.YT...N.....QALT.F.SP.AK.D....
 E.YT...ST....Q.LV...SR.AK.D....
 A.YTS..S.....Q.FA...SL.SQ.K...V
 A.YT...SV....H.FS...SQ.AK.N....
 V.YT...SQ..H.QSVT.F.TQ.PA.R....
 H.YT...TV..S.Q.LVGFLSP.P..N....
 T.Y.SV.H.SQ..RRVA.F.SP.SA.K...V
 T.T.S..H.SQI.R.VT.F.SP.SA.K...V
 K.SL..VTR..AAARLTA..SS.P..R....
 G.SL...AR..AAS.LAG..SS.P..R....
 V.Q.SPPQ.GY..SVLTGILSP.AK.N...V
 V.Q.S..Q.GY..SVLTGILSP.AK.N...V
 G.YTV..AS.F..SRLT...AL.P..R...V
 N.HTV..TEGFA.QRLT...AL.P..K....
 S.RTA..AQ.FN.Y.VA.I.SP.P..R...V
 Q.HTV..ST.HNARTLTGM.SL.AR.K....
 N.RTVA.S..A..R.FT.M.SS.SK.NL...
 Q.RTV..QVGHSVR.FT...SA.SA.N....
 E.HT..AVSGH..NVLT...SS.S..N....
 V.RT..EV....ANTFA...TT.P..N..I.
 T.YSS.QE.G..VA.FAG..TT.AK.NLY..
 S.S.V..RQ.SA.FRFT.F.SR.PT.E.K..
 N.YT.A.SM.QSIYRLTDI.ST.P..KL..V
 R.ILMA.RQ.EV.QSFGP..SLAP..K.H..
 D.YA...SV.SIMA.IARF.SP.AR.D....
 E.YA..AS.GHDVSSFAR..AP.AR.N...-
 E.HR...S...S.A.VA...TP.AR.N....
 N.RAV.MVQS...YALT...DS.AA.KL..V

(SERIDNO:65)
 45 (SERIDNO:66)
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 45 (SERIDNO:68)
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 45 (SERIDNO:70)
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 45 (SERIDNO:93)
 45 (SERIDNO:94)
 45 (SERIDNO:95)
 45 (SERIDNO:96)
 45 (SERIDNO:97)
 45 (SERIDNO:98)

FIGURE 2-2

Hutchinson Strains:		395	407	
H77	384	ETHVTGGGAGRTTAGLVGLLTGAKONIOLI	41	1977
H90		-----SVL-IASF--R-P-----		1990
HC-J4 Strains:		395	407	
HPCJ483	384	ETVTSGGGAASETTSTLASLSPGASQRIQLV	414	1983
J48711		A-----V-----RFT-----S-----		SEQ ID NO: 101
J48712		A-----AV-----RFT-P-S-----		SEQ ID NO: 102
J48713		A-----AV-----RFT-----S-----		SEQ ID NO: 103
J48714		A-----AV-----GFT-----S-----		1987
J48715		-----RV-G-----GFT-----S-----		SEQ ID NO: 104
HPCJ491		A-----V-GR-----GFT-----S-----K-----		SEQ ID NO: 105
J49120		--H-T-RV-G-----RFT-----S-----K-----		SEQ ID NO: 106
J49121		--H-T-RVVG-----GFT-----S-----K-----		SEQ ID NO: 107
J49122		--H-T-RV-GR-----GFT-----S-----K-----		1991
J49126		T-----V-GR-----GFT-----S-----K-----		SEQ ID NO: 108
J49127		K-----RFT-----		SEQ ID NO: 109
				SEQ ID NO: 110
				SEQ ID NO: 111
				SEQ ID NO: 112
NY Strains:		395	407	
NY1.1	384	STRVTGGGQGRAVHGIASLFSLGASOKIQLV	414	t ₀
NY1.2		-----Q-F-----R-----E-----		SEQ ID NO: 113
NY1.3		-----H-A-SLT-----R-----N-----		SEQ ID NO: 114
NY2.1		-----H-A-SLT-----R-----N-----		SEQ ID NO: 115
NY2.2		-----H-A-SLT-----R-----N-----		6mo
NY3.1		N-----R-----A-SLT-----P-----N-----		SEQ ID NO: 116
NY3.2		N-----R-----A-SLT-----P-----N-----		SEQ ID NO: 117
NY3.3		G-----R-----A-SLT-----P-----EN-R-----		~8mo
NY3.4		-----S-----A-SLT-----T-----N-----		SEQ ID NO: 118
NY3.5		--H--AL-----AY--T-FL-H-P-----		SEQ ID NO: 119
NY4.1		--Q-M-----AYSL-----L-P-N-----		SEQ ID NO: 120
NY4.2		--Q-M-----AYSL-----LGP-----		SEQ ID NO: 121
NY4.3		--Q-M-----AYSL-----L-P-----		14mo
				SEQ ID NO: 122
				SEQ ID NO: 123
RS Strains:		395	407	
RS1.1.	384	RTRTVGGGQVGHSVRGFTSLPESGSAQNIOLI	414	t ₀
RS1.2.		Q-----		SEQ ID NO: 124
RS1.3.		Q-----D-----		SEQ ID NO: 125
RS2.4.		Q-----L-----		SEQ ID NO: 126
RS3.1.		Q-----L-----		2mo
RS4.1.		Q-----M-G-L-----R-----		6mo
RS4.2.		Q-H-----M-G-L-----		SEQ ID NO: 127
RS5.1.		Q-H-----M-G-L-N-----		8mo
				11mo
				SEQ ID NO: 128
				SEQ ID NO: 129
				SEQ ID NO: 130
				SEQ ID NO: 131

FIGURE 3

Table 1

Amino Acid Position:		S L F G															
•	94	•	94	94	•	‡	94	‡	•	‡	•	•	•	•	•	•	•
304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321

% Conserved AA Character for Each AA Position:

40	50	58	100	100	100	97	73	77	100	75	90	100	83	89	100	99	93	100	100	87	100	100
----	----	----	-----	-----	-----	----	----	----	-----	----	----	-----	----	----	-----	----	----	-----	-----	----	-----	-----

Legend

- 99-100% identical amino acids (invariantly conserved)
- 94 100% conserved amino acid substitutions (invariantly conserved)
- 90-99% conserved amino acid substitutions
- 80-89% conserved amino acid substitutions
- ‡ 70-79% conserved amino acid substitutions
- 49-69% conserved amino acid substitutions (highly variable)

- position with the least conserved amino acid substitutions in temporally sequential time points in individual patients (Figure 3).

Notes

Positions 403 (F), 408 (G), and 407 (A, S) utilize only 2 or 3 amino acids of homologous character, respectively

Position 314 represents the only strongly conserved basic amino acid, all others conserved for hydrophobic character and/or size in the case of amino acid position 407.

Position 306 appears to be least conserved between AA 305-407 in sequentially temporal HCV isolates in individual patients (see Fig. 3).

FIGURE 4

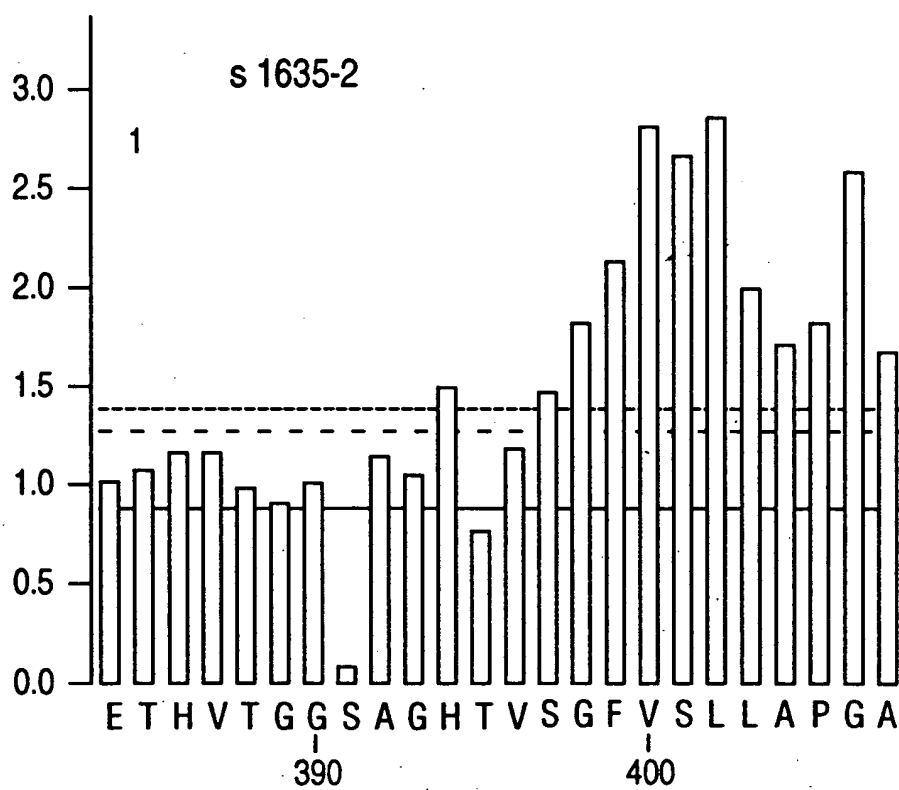
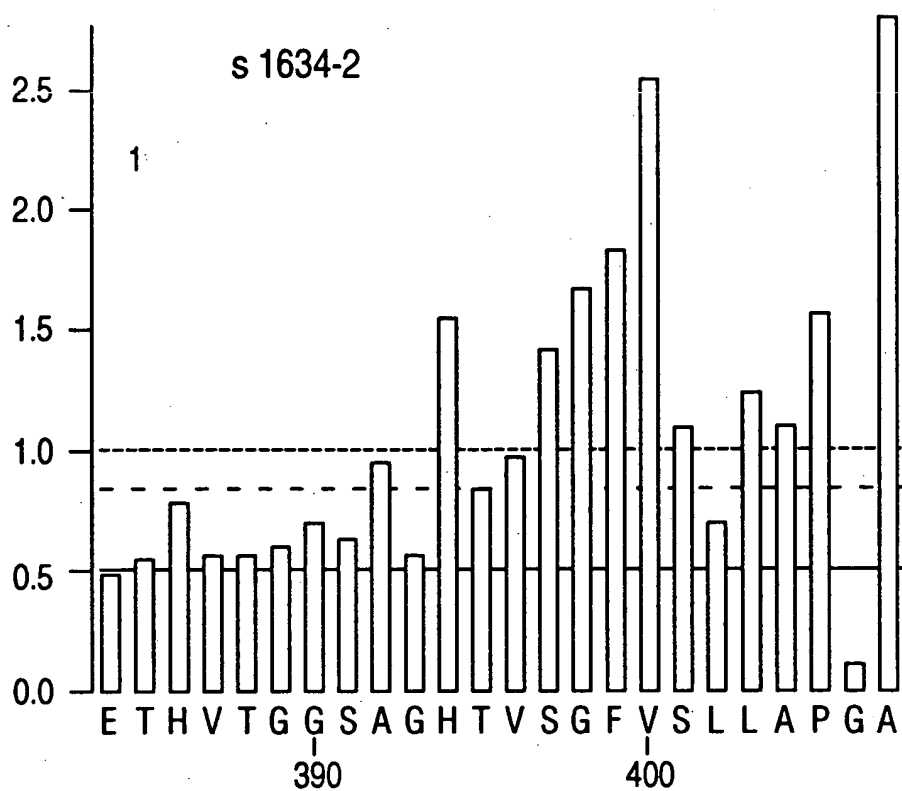


FIG. 5

824-132

B

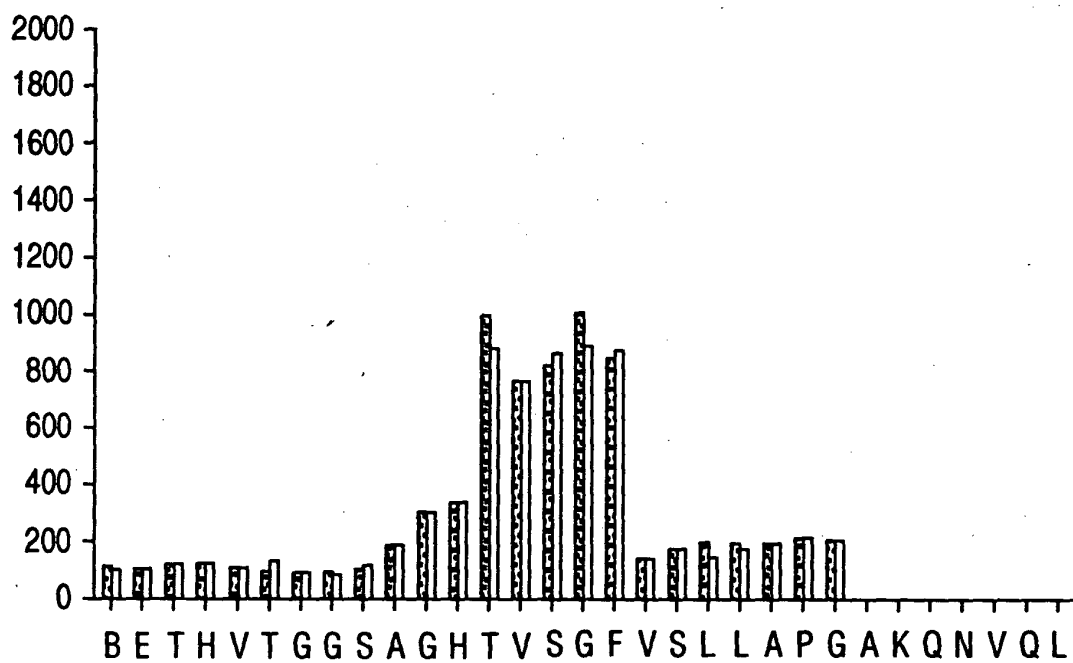


FIG. 6

76

SEQ ID NO: 133

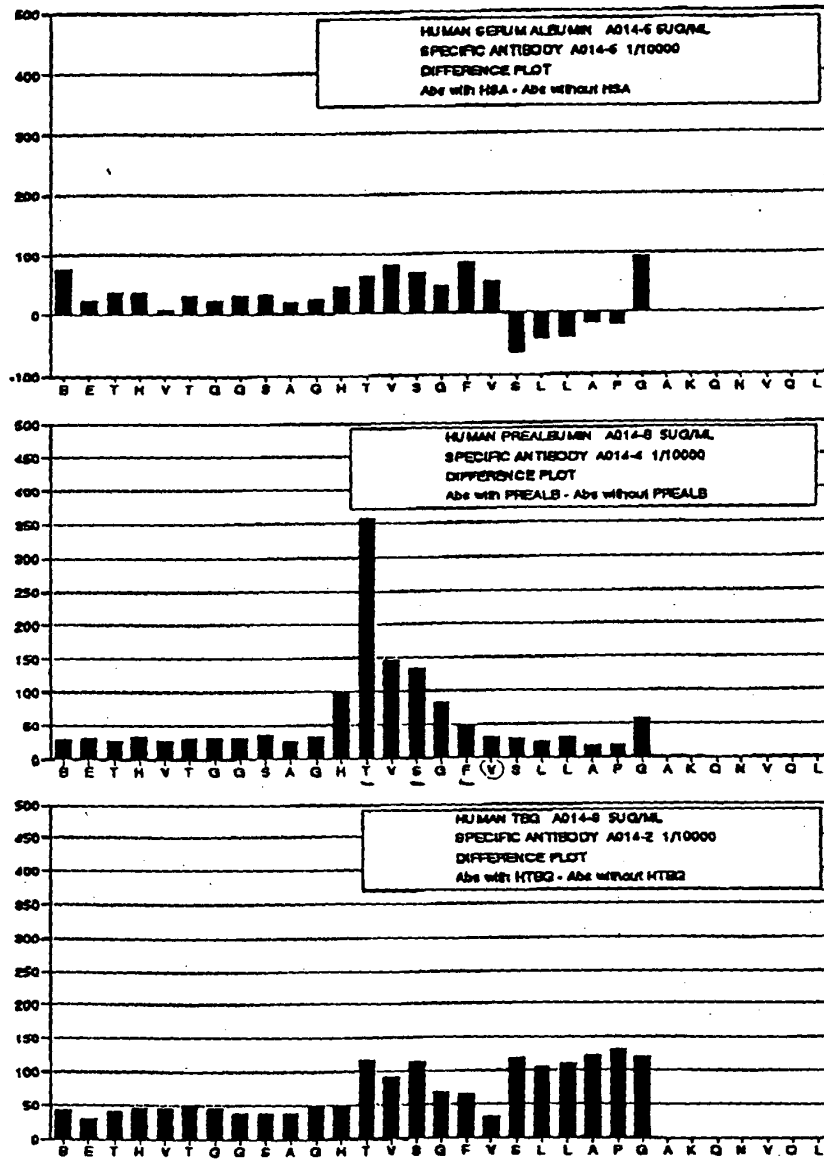


FIGURE 7

R6

SER ID NO: 133